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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,628	11/22/2004	Alberto Martin	96700/905	2223

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EXAMINER	
BURKHART, MICHAEL D	
ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
05/27/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/501,628	MARTIN ET AL.	
	Examiner	Art Unit	
	Michael Burkhart	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/4/2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,13,15,18-25,58,97,125 and 262-307* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9, 13, 15, 18-25, 58, 97, 125, and 262-307* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/4/2009 has been entered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-4, 6-9 13, 15, 19-22, 24-25, 58, 97, 125, 262-272, 276-284, and 287-307 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wabl et al (US 5,885,827, of record)

in view of Muramatsu et al (Cell, 2000, pp. 553-563, of record) as evidenced by Martin et al (PNAS, 2002, of record). **This rejection is maintained for reasons made of record in the Office Actions dated 9/13/2007, 11/14/2008, and for reasons set forth below.**

The claims (e.g. 1) have been amended to essentially replace a "gene subject to mutation" with a "DNA sequence encoding a protein." These two phrases are considered synonymous given the teachings of the prior art made of record, thus, the amendment of the claims to recite a "DNA sequence encoding a protein" or a DNA sequence encoding an antibody" (e.g. claim 58) are considered to be taught by Wabl et al for reasons made of record.

The claims (e.g. 1, 58, 97, 125) have been further amended to recite that the AID deaminates a DNA sequence, resulting in a mutation in the DNA sequence. Muramatsu et al teach that the activity of AID ultimately resulted in changes to the DNA sequence of the IgM gene under study, (page 558, ¶ bridging first and second columns to page 559, Fig. 7B, and Table 1) Muramatsu et al postulate that AID may edit DNA directly (page 561, first column, first full ¶). Furthermore, the use of AID inherently has the activity of editing DNA (Martin et al, the abstract) because, absent evidence to the contrary, it is the same enzyme and thus has the same inherent properties. The deamination of DNA is not a method step that the skilled artisan performs, rather, it is an inherent property of the use of the AID enzyme. Thus, the use of AID in the combination of Wabl and Muramatsu et al would have inherently deaminated DNA. Given the strong motivation already of record to combine the references, which does not require the knowledge of the exact activity of AID in the process of somatic hypermutation (see, e.g., pages 6-9 of the Office Action dated 11/14/2008), the fact that AID deaminates DNA directly (suggested by Muramatsu et al) does not render the instant invention non-obvious. The obvious

combination of Wabl and Muramatsu et al would have inherently created deaminated DNA by using AID, and the obviousness rejection is not predicated on knowledge of the exact activity of AID. See MPEP §2112 for a discussion of inherency:

> "The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977).";

> "There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. Schering Corp. v. Geneva Pharm. Inc., 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003)."

Claims 5 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wabl et al (5,885,827, of record) and in view of Muramatsu et al (2000, of record) as evidenced by Martin et al (2002) as applied to claims 1-4, 6-9 13, 15, 19-22, 24-25, 58, 97, 125, 262-272, 276-284, and 287-307 above, further in view of in view of Wang et al (US Patent Publication 2003/0119190, of record). **This rejection is maintained for reasons made of record in the Office Actions dated 9/13/2007, 11/14/2008, and for reasons set forth below.**

Claims 273, 274, and 275 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wabl et al (US 5,885,827, of record) and Muramatsu et al (Cell, 2000, of record) as evidenced by Martin et al (2002) as applied to claims 1-4, 6-9 13, 15, 19-22, 24-25, 58, 97, 125, 262-272, 276-284, and 287-307 above, and further in view of Griffiths (US 5,885,827, of record). **This**

rejection is maintained for reasons made of record in the Office Actions dated 9/13/2007, 11/14/2008, and for reasons set forth below.

Claims 18, 285 and 286 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wabl et al (US 5,885,827, of record) and Muramatsu et al (Cell, 2000, of record) as evidenced by Martin et al (2002) as applied to claims 1-4, 6-9 13, 15, 19-22, 24-25, 58, 97, 125, 262-272, 276-284, and 287-307 above, and further in view of Hondo et al (US Patent 6,815,194, of record). **This rejection is maintained for reasons made of record in the Office Actions dated 9/13/2007, 11/14/2008, and for reasons set forth below.**

Response to Arguments

Applicant's arguments filed 3/4/2009 have been fully considered but they are not persuasive. Applicants essentially assert: 1) a review of the Graham Factors and prior art applied on pages 13-14 of the response; 2) none of the reference applied teaches that AID edits DNA, as the exact function of AID in somatic hypermutation was unknown at the time of filing; 3) it was unknown the AID alone could affect somatic hypermutation, thus, there was no motivation to choose AID for deaminating DNA; 4) Wang, Griffiths and Honjo et al do not make up for the deficiencies of Wabl and Muramatsu et al.

Regarding 1), an analysis of the Graham Factors has been supplied in the previous Office Action, and stands for reason set forth above. Applicants review of the prior art applied is noted, but does not take into account that all of the claim limitations are taught by the prior art for

reasons made of record. Applicants assert that Muramatsu et al teach that it was unexpected that modification of AID abolished both CSR and somatic hypermutation, and postulate that AID is an RNA editing enzyme. This is not convincing for the extensive reasons made of record in the previous Office Action (referenced above) regarding the positive (and undisputed) teachings of Muramatsu et al about the role of AID in somatic hypermutation. It may have been surprising that AID played such a prominent role in CSR and somatic hypermutation *before* Muramatsu et al did their experiments, but this ignores the teachings of the remainder of Muramatsu et al. Applicants ignore that Muramatsu et al also postulate that AID may directly edit DNA (see above).

Regarding 2), see the inherency of the DNA editing activity of AID presented above, and how the combination of the references does not rely upon knowledge of the exact activity of AID in somatic hypermutation. Further, see pages 6-9 of the Office Action dated 11/14/2008 for a discussion about how the teachings of the totality prior art do not rely upon the exact activity of AID to render the claimed invention obvious.

Regarding 3), the teachings of Muramatsu et al provide convincing evidence that modifications to AID alone could cause somatic hypermutation. AID was the only enzyme modified in Muramatsu et al in order to induce somatic hypermutation of the IgM gene. Appropriate and significant reasoning and evidence have been provided to use AID of Muramatsu et al with the methods of Wabl et al, and this reasoning and evidence does not rely upon knowledge of the exact activity of AID, nor the absence or presence of other factors.

Regarding 4), Because Wabl and Muramatsu et al are deemed to not have any deficiencies for reasons set forth above, this assertion is unconvincing.

Conclusion

No claims are allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Burkhart whose telephone number is (571)272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Burkhart/
Primary Examiner, Art Unit 1633